IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CHIESI USA, INC., CORNERSTONE BIOPHARMA, INC., and EKR THERAPEUTICS, LLC, Plaintiffs, v. EXELA PHARMA SCIENCES, LLC, EXELA PHARMSCI, INC., and EXELA HOLDINGS, INC., Defendants.	)	C.A. No. 13-1275-GMS

DEFENDANTS' RESPONSIVE CLAIM CONSTRUCTION BRIEF

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I. INTRODUCTION

Plaintiff Chiesi's proposed claim construction positions are incorrect. Chiesi ignores both the relevant intrinsic evidence from the patents in suit and established canons of claim construction. For example, even though the term "pre-mixed" is directly defined in the specification, Chiesi instead relies on the specification's disclosure of a narrow alternative embodiment and the background discussion of the prior art to add five additional limitations to that term. Chiesi itself acknowledges that reading these limitations from the specification into the claims is "one of the cardinal sins of patent law." (D.I. 52 at 2, 19.) In contrast, Exela's proposed construction of "pre-mixed," which tracks exactly the definition in the specification, encompasses all the disclosed embodiments, accounts for the patentees' purported improvement over the prior art, and comports with the prosecution history. That should be the end of the matter.

Chiesi's other claim construction positions are equally suspect. Chiesi attempts to impose the requirement that the claim language relating to storage of the claimed compositions for "one year" and "three months at room temperature" be read to require an actual year or three months of storage, despite the fact that the specification, as well as the FDA and those skilled in the art, uses testing at accelerated conditions for less than three months or one year as predictive of storage for those time periods. Likewise, in its proposed construction for "buffer," Chiesi disregards the portions of the specification and the incorporated '405 Patent that conclusively demonstrate that the required buffer is a separate component from the other claimed ingredients: nicardipine, water, tonicity agent and pH adjuster (if used). Instead, for this term, and for the other terms at issue, Chiesi relies on disfavored extrinsic evidence in the form of a declaration from Dr. Klibanov that does little more than rubber stamp Chiesi's attorney argument.

Exela's proposed constructions are fully supported by the intrinsic evidence and should be adopted by the Court.

II. CHIESI'S PROPOSED CONSTRUCTIONS ARE NOT SUPPORTED BY THE INTRINSIC RECORD, WHILE CHIESI'S EXTRINSIC EVIDENCE IS UNHELPFUL AND UNNECESSARY.

A. Chiesi's Proposed Construction of "Pre-mixed Aqueous Solution" Ignores an Express Definition and Improperly Imports Extraneous Requirements.

Chiesi's construction of "pre-mixed aqueous solution" improperly narrows this claim term in ***five*** ways: (1) the construction limits the term to cover one narrow embodiment where the solution is "already mixed from the point of manufacture"; (2) it adds the extraneous limitation that the solution "is stable"; (3) it requires that the solution "allows medical personnel to use prepared containers containing an injectable formulation off the shelf without additional preparation"; (4) it mandates that the solution "avoids potential contamination problems"; and (5) it states that the solution "eliminates dosage errors." (D.I. 52 at 5-14.) The intrinsic evidence, however, does not support Chiesi's construction.

1. Exela's construction of "pre-mixed aqueous solution" covers the various embodiments disclosed in the patents in suit.

As explained in Exela's opening brief, Exela's construction of "pre-mixed aqueous solution" relies on an express definition in the patents in suit: "As used herein, the term 'pre-mixed' refers to a pharmaceutical composition that does not require reconstitution or dilution before administration to a patient." (JA Ex. A, col. 3:10-12; D.I. 56 at 7-10.) This definition is applied to pharmaceutical compositions comprising nicardipine or a nicardipine salt, at least one tonicity agent, and a buffer, all of which are required in every claim of the patents in suit. (JA Ex. A, col. 3:7-10.) Moreover, Exela's construction addresses the purported distinguishing factors over the prior art (stability, using the product without additional preparation, avoiding

contamination and eliminating dosage errors) without unnecessarily importing these factors into the construction.

Chiesi however, relies on a second, narrower definition that is found in the section of the specification relating to "Alternative Aspects." This alternative aspect relates to compositions that comprise a cardiac medication (not necessarily nicardipine), at least one of a co-solvent and a complexing agent, and a buffering agent, but which does not require a tonicity agent. (*Id.*, col. 11:13-18.) None of the claims of the patents in suit are directed to this alternative composition. For this alternative aspect, the specification states: "In this other aspect, the term 'pre-mixed', as used herein, means a pharmaceutical composition that is already mixed from the point of manufacture and does not require dilution or further processing before administration." (*Id.* at 11:25-29.)[1] Exela relies on the first, broader definition of "pre-mixed" because it relates to the claimed compositions and encompasses Chiesi's narrower definition. By contrast, Chiesi's definition from the "Alternative Aspects" section of the patents would exclude parts of the broader definition, such as when the composition is mixed after the point of manufacture of the ingredients but well before administration to a patient.

Chiesi admits that "[t]he specifications of the patents-in-suit characterize the claimed compositions as 'ready-to-use' with no reconstitution or dilution required." (D.I. 52 at 6.) Further, Chiesi actually cites to the definition proposed by Exela for the proposition that the claimed compositions differ from the prior art ampule formulations. (*Id.*) Finally, in a

[1] Notably, the Alternative Aspects section also includes a third definition of "pre-mixed" as "a pharmaceutical composition wherein the liquid solution and the active pharmaceutical ingredient are separated from the point of manufacture and in storage, such as when the solution is stored in an intravenous bag and the active pharmaceutical ingredient is lyophilized and stored in a vial that is connected to the bag, but not in fluid contact with the solution until just before administration to a patient." (JA Ex. A, col. 11:29-36.) This definition would encompass a point-of-care product. Neither party relies upon this definition as it is contrary to the claim language.

remarkable display of willful blindness, Chiesi actually claims that Exela's construction, the express definition that relates to the claimed composition, is "divorced from and inconsistent with the intrinsic record." (D.I. 52 at 1, 12.) Chiesi, however, provides no explanation as to why the inquiry should not end with the plain words of the patentees that Exela proposes. *Sinorgchem Co. v. Int'l Trade Comm'n*, 511 F.3d 1132, 1138 (Fed. Cir. 2007) (stating that it "need look no further for [the] meaning" of a term when the specification explicitly defines it).

2. Chiesi's proposed construction is not mandated by the cited portions of the specification.

Chiesi uses the narrower definition of "pre-mixed" for its proposed construction by requiring the "pre-mixed aqueous solution" to be "already mixed from the point of manufacture." (D.I. 52 at 6-7.) Chiesi's cherry-picked definition from the "Alternative Aspects" ignores the fact that it is a subset of the broader definition stated in Column 3 of the patents and that it does not relate to the compositions that are actually claimed in the patents. Where multiple definitions are provided, the broadest should control if the narrower definitions fall within the broader one. *PSN Ill., LLC v. Ivoclar Vivadent, Inc.*, 525 F.3d 1159, 1165-66 (Fed. Cir. 2008) (finding error where the district court adopted a narrow construction covering only a specific embodiment over a broader construction that covered both the embodiment and the description in the summary of invention).

In support of its contention that the compositions are "already mixed from the point of manufacture," Chiesi notes that the compositions at issue "are dispensed in pharmaceutically acceptable containers for storage and direct administration to patients." (D.I. 52 at 6-7; JA Ex. A, col. 2:35-37.) Nothing about the fact that that the compositions are contained in pharmaceutically acceptable containers for storage and direct administration to patients contradicts Exela's definition. Despite Chiesi's assertion to the contrary, nothing in the

specification mandates that the mixing/diluting may not take place in a pharmacy, hospital or otherwise for storage at some point prior to the need for administration to a patient.

Moreover, Chiesi criticizes Exela's construction as covering the prior art ampules/point of care formulations. (D.I. 52 at 12.) That is not correct. Exela's proposed construction explicitly says that dilution or reconstitution is not required, unlike with the prior art ampule/point of care formulations.

Chiesi incorrectly argues that Exela's construction renders superfluous the claim term "wherein the aqueous solution requires no dilution before administration" in two claims out of sixty-six claims in the patents in suit. (*Id.* at 13.) This argument is inconsistent with Chiesi's reliance on the definition of "pre-mixed" provided in the "Alternative Aspects" section of the patents. That definition also states that the composition does not require dilution or further processing (such as reconstitution) before administration. (JA Ex. A, col. 11:25-29.) Moreover, the Federal Circuit has recognized that "surplusage may exist in some claims" where the surplusage is necessary to arrive at the proper construction of a claim term – particularly where the intrinsic evidence expressly defines the term. *ERBE Elektromedizin GmbH v. Canady Tech. LLC*, 629 F.3d 1278, 1286 (Fed. Cir. 2010) (rejecting surplusage argument where prosecution history required the definition); *see also Pickholtz v. Rainbow Techs., Inc.*, 284 F.3d 1365, 1373 (Fed. Cir. 2002) (finding that a construction was appropriate based on the intrinsic record though it created surplusage).

Chiesi also asserts that the definition of "pre-mixed aqueous solution" should be limited to require that the compositions are "stable," can be used "off the shelf without additional preparation," "avoid[] potential contamination problems," and "eliminate[] dosage errors." (D.I. 52 at 5, 7-8.) Exela does not dispute that the specifications disclose certain alleged benefits of

the invention over the prior art. Patents frequently discuss the ways in which the claimed invention is an improvement over the prior art. However, this does not require every alleged benefit of the invention be imported into the claims or into a particular claim limitation. In fact, as Chiesi itself notes, reading limitations from the specification into the claims is "one of the cardinal sins of patent law." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1319-20 (Fed. Cir. 2005). "Where a specification does not require an extraneous limitation, that limitation should not be read from the specification into the claims." *Anheuser-Busch Cos. v. Crown Cork & Seal Techs. Corp.*, 121 Fed. Appx. 388, 393 (Fed. Cir. 2004).

3. The prosecution of the patents in suit supports Exela's construction, not Chiesi's construction.

Exela's proposed construction of "pre-mixed aqueous solution" is supported by the prosecution of the patents in suit. The provisional patent application for U.S. Patent Application No. 60/793,074 ("the '074 Application"), the application to which the patents in suit claim priority, related only to the "Alternative Aspects" composition: one containing a cardiac agent, at least one of a co-solvent and a complexing agent, and a buffer, but not requiring a tonicity agent. (JA Ex. E, A-96:2-9.) Thus, the applicants defined "pre-mixed" using only the narrow definition that is now found in Column 11 of the patents in suit. (*Id.* at A-96:15-17.) The specifications of the patents in suit, however, are not so limited. They were expanded to include a different composition, one where the cardiac agent is nicardipine, and where the composition also must contain a tonicity agent along with nicardipine hydrochloride and a buffer. It is to this composition that the broader definition of "pre-mixed" that now appears in Column 3 of the specifications relates. This indicates a clear intent by the patentees to broaden the definition of "pre-mixed aqueous solution" beyond the original position that the solution was "already mixed from the point of manufacture."

Further, Chiesi's assertion that it disclaimed point of care dosage forms during prosecution has no bearing on the proper construction of "pre-mixed aqueous solution." (D.I. 52 at 8-11.) Chiesi argues that because the patentees described the benefits of the claimed compositions during prosecution as compared to the prior art concentrated ampule formulation, these benefits should be incorporated into the definition of "pre-mixed aqueous solution."[2] (*Id.*) This is incorrect for several reasons. First, the fact that the patentees noted deficiencies in the prior art during the prosecution of the patents in suit does not require the alleged benefits to be incorporated into the definition of "pre-mixed aqueous solution." *See i4i Ltd. P'shp v. Microsoft Corp.*, 598 F.3d 831, 843 (Fed. Cir. 2010) ("[N]ot every benefit flowing from an invention is a claim limitation."); *Kim v. ConAgra Foods, Inc.*, 465 F.3d 1312, 1318-19 (Fed. Cir. 2006) (rejecting a construction incorporating an object of the invention).

Second, these statements in the prosecution history are consistent with Exela's construction. It is clear from the specification and the express definition of "pre-mixed" relied upon by Exela that the claims do not cover the prior art concentrated ampule formulation, which required reconstitution or dilution before administration to a patient. (D.I. 56 at 8-9.) Exela's proposed construction recognizes this distinction between the claimed invention and the prior art. In this regard, the present situation is similar to the *Kinik* decision cited by Chiesi. (D.I. 52 at 10.) In *Kinik*, the Federal Circuit found that the proper construction of "liquid binder" was dictated by statements in the patent's specification that limited the claim scope, and that construction was merely confirmed by the prosecution history. *Kinik Co. v. Int'l Trade Comm'n*, 362 F.3d 1359, 1364-66 (Fed. Cir. 2004). Similarly here, the specification provides an express definition of "pre-mixed" that excludes the prior art concentrated ampule, and the prosecution

[2] This argument is unique as it is almost always the case the disclaimer is urged by the accused infringer, not the patentee.

history just confirms that position – there is no disavowal. This case is thus distinguishable from the *Omega Engineering* and *Rheox* cases, where the claims arguably could be construed to cover the prior art after reviewing the specification but such coverage was disavowed during prosecution. *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1322-23, 1326-27 (Fed. Cir. 2003) (finding the term "to visibly outline" to include requirement that no energy is infused due to prosecution argument that prior art allowed infusion); *Rheox, Inc. v. Entact, Inc.*, 276 F.3d 1319, 1322-27 (Fed. Cir. 2002) (finding a particular species described as "calcium orthophosphate" in the specification was not encompassed by that claim term because explicit reference to that species had been removed from the claim during prosecution to overcome prior art).

Further, Exela's construction is not in conflict with the *MBO Laboratories* case cited by Chiesi. (D.I. 52 at 10, 13.) *MBO Labs* stands for the unremarkable proposition that "prosecution arguments . . . which draw distinctions between the patented invention and the prior art are useful for determining whether the patentee intended to surrender territory, since they indicate in the inventor's own words what the invention is not." *MBO Labs, Inc. v. Becton, Dickinson & Co.*, 474 F.3d 1323, 1330 (Fed. Cir. 2007). As Exela's construction accounts for the problems with the prior art, it is consistent with the dictates of *MBO Labs*.

4. Chiesi's extrinsic evidence in the form of purported expert testimony is unnecessary and unhelpful.

The extrinsic evidence declaration of Chiesi's expert, Dr. Klibanov, is not useful to the Court in construing the claims and should be accorded no weight. *Sinorgchem*, 511 F.3d at 1137 n.3 (attributing no weight to conclusory expert testimony of what a person of ordinary skill would understand without evidence that the term had an accepted meaning in the field); *Network Commerce, Inc. v. Microsoft Corp.*, 422 F.3d 1353, 1361 (Fed. Cir. 2005) (finding expert

testimony that relied only on specification, without other evidence, was unhelpful); *Phillips*, 415 F.3d at 1318 ("[C]onclusory, unsupported assertions by experts as to the definition of a claim term are not useful to a court."). As an initial matter, Dr. Klibanov's declaration does little more than recite portions of the specification and prosecution history describing the benefits of the claimed compositions or describing the shortcomings of the prior art. (*E.g.*, D.I. 53, ¶¶ 24-26, 31-32.) Dr. Klibanov then provides his view of the construction, as if he were providing a legal interpretation. Indeed, Dr. Klibanov's proffered analysis declaration is mere repetition of the arguments made in Chiesi's brief.

Dr. Klibanov's testimony is also contrary to the full scope of the intrinsic record. For example, Dr. Klibanov does not directly address the primary, express definition of "pre-mixed" set forth in Column 3 of the specifications. (JA Ex. A, col. 3:10-12.) Instead, he focuses his analysis of "pre-mixed aqueous solution" on the inventors' distinctions between the compositions at issue and the prior art, and how these distinctions should be used to place limitations on the express definition provided by the specification. (*E.g.* D.I. 53, ¶¶ 29-32). Extrinsic evidence like Dr. Klibanov's testimony has no value in trying to limit the construction of claims terms in ways that contradict the intrinsic evidence. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996).

B. The "Room Temperature" Terms Do Not Require Construction.

Chiesi contends that the terms "one year at room temperature" and "three months at room temperature" should have the phrase "full-term" tacked on to mean "one year full-term at room temperature" and "three months full-term at room temperature." (D.I. 52 at 14-16.) Presumably, Chiesi seeks to exclude formulations whose stability has been measured using accelerated testing (a common technique in the industry) from the scope of its claims. (Myrdal Decl. ¶¶ 15-18.)

Whether or not accelerated testing data meets the "for one year at room temperature" or "for three months at room temperature" is a question of fact for the factfinder to resolve, not a question of claim construction. These terms do not require construction by the Court because they are clear on their face and should be given their plain and ordinary meaning. (D.I. 56 at 1 n.1.)

To support its inclusion of "full-term" in the definition of the "room temperature" terms, Chiesi points to a prior art reference cited in Example 2 of the specifications of the patents in suit. (JA Ex. A, col. 15:1-9.) The reference merely states that conclusions drawn about stability of a product using accelerated stability data should be confirmed using "full-term" studies. (JA Ex. I at A-174.) Accelerated stability testing is generally done above room temperature for a shorter time period to predict the stability of a composition at room temperature over a longer period. (Myrdal Decl. ¶ 15.) The patents in suit do not state or suggest that accelerated testing is inappropriate or should not be used to evaluate stability. This type of testing is commonly used in the industry, and, in fact, the prior art reference cited by the patents states that "short-term accelerated studies *should be* carried out." (JA Ex. I at A-173 (emphasis added); Myrdal Decl. ¶¶ 15-17.)

The stability data shown in the specifications also demonstrates that Chiesi's construction is inappropriate. Example 2, from which Chiesi's reference is drawn, uses accelerated stability data to determine the effect of pH on stability. The other examples also demonstrate use of accelerated testing conditions to measure stability. (*E.g.* JA Ex. A, col. 15:66-16:4, 22:42-49, 23:41-49.) There is no stability data in the specifications covering an extended period. Only one example uses room temperature data from an extended period (*Id.* at 17:19-25), suggesting that the higher temperatures used in the other examples represent accelerated testing conditions.

Nothing in the specifications requires that the stability of the compositions be measured in a particular way. Dr. Klibanov's unsupported assertion that a person of ordinary skill would understand the "at room temperature" limitations to mean "full term" cannot be used to contradict the specifications.

Chiesi's construction is also contrary to accepted practice in the pharmaceutical manufacturing industry. Applicants frequently use "accelerated" stability data in submissions to the U.S. Food and Drug Administration ("FDA"). (Myrdal Decl. ¶ 18.) The FDA has published a Guidance describing common methods for evaluating stability including exposure of compositions to conditions designed to increase change in the drug substance or drug product in order to assess longer term effects to the compositions under non-accelerated conditions. (Myrdal Decl., Ex. C at 6, 9-10.) The FDA Guideline requires accelerated testing data be provided for new drug substances/products. (*Id.* at 4, 6.)

The Court should reject Chiesi's proposed construction and leave the fact finder to determine whether these limitations are met by any composition placed at issue.

C. The "Buffer" Terms Should Be Construed to Require a Separate and Distinct Buffer

Chiesi's proposed construction for the buffer limitations ("a system capable of maintaining the pH within an optimal range") is improper because it (1) encompasses compositions in which the buffer would not be a separate and distinct component of the composition and (2) ignores that the buffer must maintain the optimal pH range throughout the shelf life of the product. (D.I. 52 at 16-20.) The plain language of the claims and the specifications dictate a contrary conclusion.

1. Exela's proposed construction of the "buffer" limitations is dictated by the intrinsic evidence.

As Exela explained in its opening brief, the intrinsic evidence demonstrates that the proper construction of the "buffer" limitations requires the buffer to be a separate and distinct component that maintains the optimal pH range throughout the shelf life of the product. (D.I. 56 at 10-17.) The claim language, common specification and '405 Patent (which is intrinsic evidence) repeatedly distinguish between the various components of the compositions, thereby dictating that a buffer is a component "separate and distinct from nicardipine hydrochloride, tonicity agent, cosolvent, water and/or pH adjuster." (*Id.*) The same intrinsic evidence shows that the buffer system maintains the desired pH range for the product. (*Id.* at 13-14, 16.)

2. Chiesi's proposed construction ignores the requirements of the claims and the patent specifications.

Chiesi's assertion that the intrinsic evidence does not require the buffer to be "separate and distinct" from the other elements of the composition fails upon closer examination. For example, the claims of the patents in suit recite the buffer as a component[3] separate from nicardipine, the tonicity agent, the co-solvent, water and the pH adjuster. (*E.g.*, JA Ex. A, col. 27:59–28:28.) When limitations are separately listed, like "buffer" and "pH adjuster," it is a "clear implication" that the limitations represent distinct components of the invention. *Becton, Dickinson & Co. v. Tyco Healthcare Group LP*, 616 F.3d 1249, 1254 (Fed. Cir. 2010). This is also shown by the doctrine of claim differentiation, which presumes that different claims have different meanings. Here, for example, claim 1 of the '102 patent requires among other things,

[3] Chiesi argues via Dr. Klibanov that Exela's definition is incorrect because a buffer may be a mixture of substances. (D.I. 53 at ¶¶ 60-61.) This argument is based on the incorrect assumption that a "component" can be only one ingredient. This is not the case—the buffer component can be made of more than one ingredient that when mixed together forms a buffer. Those ingredients just must be something different from the nicardipine, tonicity agent, co-solvent, water and pH adjuster.

nicardipine hydrochloride, a tonicity agent, and a buffer. (JA Ex. A, col. 27:59–28:28.) Claim 4 is dependent on claim 1, and requires that the composition "further compris[es] at least one pH adjuster." *Phillips*, 415 F.3d at 1314-15 ("[T]he presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim.") Thus the plain language of the claims themselves demonstrate that the buffer is a component distinct from the other components recited in the claim including the nicardipine hydrochloride, tonicity agent, cosolvent, water or pH adjuster.

Table 1 of the common specification identifies eight compositions and separately lists the components that constitute the active ingredient (nicardipine hydrochloride), the tonicity agent(s), the co-solvent, and the buffer for each. (JA Ex. A, col. 8:1-25.) In all instances, citric acid was listed as the buffer but was not listed as any of the active ingredient, tonicity agent(s) or co-solvent. (*Id.*) Every description of the compositions in the specifications lists the buffer as a separate component of the composition. (*E.g.*, *id.* at col. 2:10-13, 7:65–8:25, 8:65–9:32, 11:13-17.)

Chiesi, however, argues that the buffer cannot be separate and distinct because the patents in suit also identify "citric acid" as a "pH adjuster" in addition to it being a buffer. (D.I. 52 at 18.) The fact that citric acid could be used as a pH adjuster does not undermine the consistent discussion throughout the specification that the buffer is separate from nicardipine hydrochloride, the tonicity agent, water, the co-solvent or the pH adjuster. (JA Ex. A, col. 2:10-13, 3:7-24, 8:1–9:32, 11:13-18.) For example, the patents discuss how the claimed compositions are made. In every instance, the buffer is added as a separate component from the nicardipine hydrochloride, tonicity agent, co-solvent, and pH adjuster. (*Id.* at col. 8:32-9:32.) In fact, all of

the embodiments relating to the use of citric acid as a buffer state that the pH may also be adjusted, *i.e.,* a pH adjuster may be added. (*Id.* at col. 8:65-9:14.)

This point is reinforced by the fact that the common specification states that a pH adjuster can be added "if required." (*Id.* at col. 2:33-35.) If the claimed buffer is not a separate and distinct component from the claimed pH adjuster, the optional "if required" language in the specification would be obviated. That is not the correct reading of the claim in light of the specification. It does not say that where citric acid is the buffer, it can also do "double duty" as the pH adjuster. Rather, the correct reading is that the claimed buffer is a separate and distinct component from a pH adjuster that can be added "if required" to adjust the pH.

Chiesi's construction of the "buffer" limitations also contradicts the specification of the '405 Patent, which is intrinsic evidence because it is incorporated into the patents in suit by reference. The common specification of the patents in suit states that the '405 Patent "describes a *buffered* pharmaceutical composition containing nicardipine designed for parenteral administration." (*Id.* at col 1:35-38 (emphasis added).) Examples A and B in the '405 Patent, however, contain nicardipine hydrochloride (the active ingredient), sodium chloride (a tonicity agent), sorbitol (a tonicity agent), hydrochloric acid (a pH adjuster) and water for injection – but no buffer. (JA Ex. K, col. 5:50-6:41, 7:32-40 (Table 1).)

As discussed on pages 15-17 of Exela's opening brief, the '405 patentees found the unbuffered Example B formulation to be "unsatisfactory" and "it was conceived to **add** a dilute buffer solution" to overcome the problems with the formulation. (*Id.* at col. 6:3-5, 40-45 (emphasis added).) That is, a component *in addition to* nicardipine hydrochloride, sodium chloride, sorbitol, hydrochloric acid and water for injection was separately added to buffer the solution. This description in the '405 Patent of adding a separate buffering component to

parenteral nicardipine compositions clearly informs the proper construction of the term "buffer" in the claims of the patents in suit.

Chiesi notes that the '074 Application, to which the patents in suit claim priority, states that "[b]uffering agents are used to adjust the pH of the pharmaceutical compositions." (JA Ex. E at A101.) This statement, which relates to the unclaimed "Alternative Aspect" compositions, is not technically accurate in this instance because the examples shown in the common specification contain a pH adjuster (hydrochloric acid), and should not be used to contradict the rest of the intrinsic evidence. This is especially the case where this language was later *removed* from the '076 Application (the application that resulted in the '102 Patent), from which all of the patents in suit arise. Furthermore, the common specification states that the purpose of the buffer is not only to ensure that the composition falls within the optimal pH range, but that it *remains there* as well. (JA Ex. A, col. 4:20-24.) To accomplish this purpose, a particular component with sufficient buffering capacity has to be separately added to the claimed composition. Alternatively, even if one were to assume, for the sake of argument, that the buffer can perform multiple functions and also serve as the pH adjuster, it still remains clear that the buffer cannot be any of the components identified as "Unsatisfactory Prior Art Formulations" in Examples A and B/Table 1 of the '405 Patent. The '405 Patent is clear that the formulations in Table 1 contain no buffer.

Finally, Chiesi's citation to Exela's construction of "a buffering agent" in *Cadence Pharmaceuticals v. Paddock Laboratories, Inc.* is a red herring with no relevance to the instant analysis. That case involved different claims with a different specification. The construction dictated by the intrinsic record in that case is of no moment to the construction dictated by the

intrinsic record in this case. Chiesi's construction is inconsistent with the words of the specification and the "clear implication" of the claims and should therefore be rejected.

3. The buffer's pH control is what determines the composition's shelf-life and is therefore a necessary part of the proper construction of the buffer limitations.

Chiesi asserts that a buffer need not maintain the pH of the composition for the entirety of its shelf-life. (D.I. 52 at 19-20.) This conflicts with the fundamental purpose of the buffer in the claimed compositions. Indeed, the specification specifically states that the buffer has "sufficient buffering capacity to maintain the desired pH range throughout the shelf-life of the product."[4] (JA Ex. A, col. 4:20-24.) The specification further discloses that the stability of the nicardipine compositions at issue is significantly impacted by the pH of the solution. (*Id.* at col. 15:23-26.) Control of the pH is necessary to keep the nicardipine active ingredient in solution and prevent the formation of impurities, i.e. to maintain stability. (*Id.* at col. 4:24-26; JA Ex. K, col. 4:26-32, 4:57-62.) The buffer maintains the pH in the range optimal for the stability of the compositions. (JA Ex. A, col. 3:10-21, 4:26-32.) Shelf-life is the amount of time for which the stability of the composition is maintained. The buffer maintaining the pH in the optimal range is what defines the shelf life of the composition. That is, if the buffer did not maintain the pH within the optimal range, loss of nicardipine and formation of impurities would increase and the composition would no longer maintain the required stability, ending its shelf-life. Thus, requiring that the buffer maintain the optimal pH "throughout the shelf-life of the product" is consistent with the buffer's purpose in the claimed compositions.

[4] Chiesi's construction of "buffer" would only have the buffer be "capable of maintaining" the pH. (D.I. 52 at 16.) This is inconsistent with the statement in the common specification that the buffer "maintain[s]" the pH, not just that it be capable of doing so. (JA Ex. A, col. 4:20-24.). Exela's construction is consistent with the specification.

Chiesi points to claims 8 and 9 of the '102 Patent as only requiring the maintenance of drug potency and limitation of impurity formation for three months. (D.I. 52 at 19.) Chiesi argues that this means the buffer need not maintain the optimal pH throughout the composition's shelf-life. However, maintenance of these stability indicators within the specified ranges defines what the shelf-life is. Chiesi's construction begs the question of how long the buffer must maintain the optimal pH range. Its reliance on the "three months" seems to suggest that maintaining the pH within the optimal range for any amount of time could be sufficient. Chiesi states that Exela's construction ignores "numerous other disclosures that do ***not*** require pH to be maintained throughout the shelf-life" but points to only one example. The only passage in the specification which describes the length of time for which the pH must be maintained within the optimal range is "throughout the shelf-life of the product." (JA Ex. A, col 4:20-24.)

The Court thus should reject Chiesi's proposed construction of the "buffer" limitations and adopt Exela's construction based on the intrinsic evidence.

4. Chiesi again relies on unnecessary extrinsic evidence to support its improper construction of the "buffer" limitations.

As with its construction of "pre-mixed aqueous solution," Chiesi cites to the declaration of Dr. Klibanov to support its construction of the "buffer" limitations. (D.I. 52 at 17-20.) Dr. Klibanov's support of Chiesi's construction contradicts the unambiguous intrinsic evidence because it encompasses components that were specifically declared not to be buffers in injectable nicardipine solutions. For example, Dr. Klibanov ignores the fact that the '405 Patent, noted *supra* in Section II.C.1, is express in its teaching that nicardipine hydrochloride, the tonicity agent, the co-solvent, water and the pH adjuster are not buffers or at the very least the specific components shown in Examples A and B of the '405 Patent are not buffers. Therefore, Dr. Klibanov's opinion contradicts the intrinsic record and should be entitled to no weight. *Vitronics*

Corp., 90 F.3d at 1584 ("However, as we have recently re-emphasized, extrinsic evidence in general, and expert testimony in particular, may be used only to help the court come to the proper understanding of the claims; it may not be used to vary or contradict the claim language. Nor may it contradict the import of other parts of the specification. Indeed, where the patent documents are unambiguous, expert testimony regarding the meaning of a claim is entitled to no weight.") (internal citation omitted).

Additionally, Dr. Klibanov's assertion that a person of ordinary skill would understand that components of a pharmaceutical composition can serve more than one purpose is both irrelevant and contrary to the intrinsic evidence, and thus entitled to no weight. *Id*. As noted above, whether a component of a pharmaceutical can generally serve more than one purpose is irrelevant because the specification in this case requires the buffer be a separate component from the other listed components.

III. CONCLUSION

For the foregoing reasons, Exela respectfully asks that the Court reject Chiesi's proposed claim constructions.

Respectfully submitted,

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CERTIFICATE OF SERVICE

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